



Contents lists available at ScienceDirect

Asian Pacific Journal of Tropical Biomedicine

journal homepage: www.elsevier.com/locate/apjtb

Document heading

doi:10.1016/S2221-1691(13)60075-1

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A review on therapeutic potential of *Nigella sativa*: A miracle herbAftab Ahmad^{1*}, Asif Husain², Mohd Mujeeb³, Shah Alam Khan⁴, Abul Kalam Najmi⁵, Nasir Ali Siddique⁶, Zoheir A. Damanhour⁷, Firoz Anwar⁸¹Health Information Technology Department, Jeddah Community College, King Abdulaziz University, Jeddah-21589, Kingdom of Saudi Arabia²Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Hamdard University, New Delhi, India³Department of Pharmacognosy, Faculty of Pharmacy, Hamdard University, New Delhi, India⁴Oman Medical College, Muscat, Sultanate of Oman⁵Department of Pharmacology, Faculty of Pharmacy, Hamdard University, New Delhi-110062, India⁶Department of Pharmacognosy, College of Pharmacy, King Saud University, Riyadh-11451, Saudi Arabia⁷Department of Pharmacology, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia⁸Siddhartha Institute of Pharmacy, Dehradun, Uttarakhand, India

PEER REVIEW

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Comments

The current review on *Nigella* provides the detailed scientific information of this medicinal plant. Due to its miraculous medicinal properties *N. sativa* has been widely used as antihypertensive, liver tonics, diuretics, digestive, anti-diarrheal, appetite stimulant, analgesics, anti-bacterial and in skin disorders. Extensive studies on *N. sativa* have been carried out by various researchers and a wide spectrum of its pharmacological actions have been explored, including antidiabetic, anticancer, immunomodulator, analgesic, antimicrobial, anti-inflammatory, spasmolytic, bronchodilator, hepatoprotective, renal protective, gastroprotective and antioxidant properties.

(Details on Page 349)

ABSTRACT

Nigella sativa (*N. sativa*) (Family Ranunculaceae) is a widely used medicinal plant throughout the world. It is very popular in various traditional systems of medicine like Unani and Tibb, Ayurveda and Siddha. Seeds and oil have a long history of folklore usage in various systems of medicines and food. The seeds of *N. sativa* have been widely used in the treatment of different diseases and ailments. In Islamic literature, it is considered as one of the greatest forms of healing medicine. It has been recommended for using on regular basis in Tibb-e-Nabwi (Prophetic Medicine). It has been widely used as antihypertensive, liver tonics, diuretics, digestive, anti-diarrheal, appetite stimulant, analgesics, anti-bacterial and in skin disorders. Extensive studies on *N. sativa* have been carried out by various researchers and a wide spectrum of its pharmacological actions have been explored which may include antidiabetic, anticancer, immunomodulator, analgesic, antimicrobial, anti-inflammatory, spasmolytic, bronchodilator, hepato-protective, renal protective, gastro-protective, antioxidant properties, etc. Due to its miraculous power of healing, *N. sativa* has got the place among the top ranked evidence based herbal medicines. This is also revealed that most of the therapeutic properties of this plant are due to the presence of thymoquinone which is major bioactive component of the essential oil. The present review is an effort to provide a detailed survey of the literature on scientific researches of pharmacognostical characteristics, chemical composition and pharmacological activities of the seeds of this plant.

KEYWORDS

Nigella sativa, Miracle herb, Ranunculaceae, Habat-ul-Sauda, Thymoquinone, Tibb-e-Nabwi, Black seeds, Anti-diabetic, Antioxidant

1. Introduction

Medicinal plants have been used for curing diseases for many centuries in different indigenous systems of medicine as well as folk medicines. Moreover, medicinal plants are also used in the preparation of herbal medicines as they are considered to be safe as compared to modern allopathic medicines. Many

researchers are focusing on medicinal plants since only a few plant species have been thoroughly investigated for their medicinal properties, potential, mechanism of action, safety evaluation and toxicological studies.

Among various medicinal plants, *Nigella sativa* (*N. sativa*) (Family Ranunculaceae) is emerging as a miracle herb with a rich historical and religious background since many

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Foundation Project: Supported by Deanship of Scientific Research, King Abdulaziz University, Jeddah, Saudi Arabia (Grant No. 431-044).

Article history:

Received 8 Mar, 2013

Received in revised form 18 Mar, 2nd revised form 26 Mar, 3rd revised form 7 Apr 2013

Accepted 18 Apr 2013

Available online 28 May 2013

researches revealed its wide spectrum of pharmacological potential. *N. sativa* is commonly known as black seed. *N. sativa* is native to Southern Europe, North Africa and Southwest Asia and it is cultivated in many countries in the world like Middle Eastern Mediterranean region, South Europe, India, Pakistan, Syria, Turkey, Saudi Arabia^[1].

The seeds of *N. sativa* and their oil have been widely used for centuries in the treatment of various ailments throughout the world. And it is an important drug in the Indian traditional system of medicine like Unani and Ayurveda^[2,9]. Among Muslims, it is considered as one of the greatest forms of healing medicine available due to it was mentioned that black seed is the remedy for all diseases except death in one of the Prophetic hadith. It is also recommended for use on regular basis in Tibb-e-Nabwi (Prophetic Medicine)^[3].

N. sativa has been extensively studied for its biological activities and therapeutic potential and shown to possess wide spectrum of activities viz. as diuretic, antihypertensive, antidiabetic, anticancer and immunomodulatory, analgesic, antimicrobial, anthelmintics, analgesics and anti-inflammatory, spasmolytic, bronchodilator, gastroprotective, hepatoprotective, renal protective and antioxidant properties. The seeds of *N. sativa* are widely used in the treatment of various diseases like bronchitis, asthma, diarrhea, rheumatism and skin disorders. It is also used as liver tonic, digestive, anti-diarrheal, appetite stimulant, emmenagogue, to increase milk production in nursing mothers to fight parasitic infections, and to support immune system^[4–9]. Most of the therapeutic properties of this plant are due to the presence of thymoquinone (TQ) which is a major active chemical component of the essential oil. Black seeds are also used in food like flavoring additive in the breads and pickles because it has very low level of toxicity^[10].

2. Pharmacognostical characteristics

2.1. Morphology of the plant

N. sativa is an annual flowering plant which grows to 20–90 cm tall, with finely divided leaves, the leaf segments narrowly linear to threadlike. The flowers are delicate, and usually colored white, yellow, pink, pale blue or pale purple, with 5–10 petals. The fruit is a large and inflated capsule composed of 3–7 united follicles, each containing numerous seeds^[9,11].



Figure 1. *N. sativa* (whole plant, flower and seeds) adopted from internet.

2.2. Characteristics of the seeds and powder

Macroscopically, seeds are small dicotyledonous, trigonous, angular, regulose-tubercular, 2–3.5mm×1–2 mm, black externally and white inside, odor slightly aromatic and taste bitter. Microscopically, transverse section of seed shows single layered epidermis consisting of elliptical, thick walled cells, covered externally by a papillose

cuticle and filled with dark brown contents. Epidermis is followed by 2–4 layers of thick walled tangentially elongated parenchymatous cells, followed by a reddish brown pigmented layer composed of thick walled, rectangular elongated cells. Inner to the pigment layer, is present a layer composed of thick walled rectangular elongated or nearly columnar, elongated cells. Endosperm consists of thin walled, rectangular or polygonal cells mostly filled with oil globules. The powder microscopy of seed powder shows brownish black, parenchymatous cells and oil globules^[1,11].

3. Chemical composition of black seeds

Many active compounds have been isolated, identified and reported so far in different varieties of black seeds. The most important active compounds are thymoquinone (30%–48%), thymohydroquinone, dithymoquinone, p-cymene (7%–15%), carvacrol (6%–12%), 4-terpineol (2%–7%), t-anethol (1%–4%), sesquiterpene longifolene (1%–8%) α -pinene and thymol *etc.* Black seeds also contain some other compounds in trace amounts. Seeds contain two different types of alkaloids; i.e. isoquinoline alkaloids *e.g.* nigellicimine and nigellicimine-N-oxide, and pyrazol alkaloids or indazole ring bearing alkaloids which include nigellidine and nigellicine. Moreover, *N. sativa* seeds also contain α -hederin, a water soluble pentacyclic triterpene and saponin, a potential anticancer agent^[12,13].

Some other compounds *e.g.* carvone, limonene, citronellol were also found in trace amounts. Most of the pharmacological properties of *N. sativa* are mainly attributed to quinine constituents, of which TQ is the most abundant. On storage, TQ yields dithymoquinone and higher oligocondensation products. The seeds of *N. sativa* contain protein (26.7%), fat (28.5%), carbohydrates (24.9%), crude fibre (8.4%) and total ash (4.8 %). The seeds are also containing good amount of various vitamins and minerals like Cu, P, Zn and Fe *etc.* The seeds contain carotene which is converted by the liver to vitamin A. Root and shoot are reported to contain vanillic acid^[12,14].

The seeds reported to contain a fatty oil rich in unsaturated fatty acids, mainly linoleic acid (50–60%), oleic acid (20%), eicodadienoic acid (3%) and dihomolinoleic acid (10%). Saturated fatty acids (palmitic, stearic acid) amount to about 30% or less. α -sitosterol is a major sterol, which accounts for 44% and 54% of the total sterols in Tunisian and Iranian varieties of black seed oils respectively, followed by stigmasterol (6.57–20.92% of total sterols)^[15–17].

Examples of various other reported chemical components includes nigellone, avenasterol-5-ene, avenasterol-7-ene, campesterol, cholesterol, citrostadienol, cycloeculenol, gramisterol, lophenol, obtusifoliol, stigmastanol, stigmasterol-7-ene, β -amyirin, butyrospermol, cycloartenol, 24-methylene-cycloartenol, taraxerol, tirucallol, 3-O- $[\beta$ -D-xylopyranosyl(1 $\rightarrow$ 3)- α -L-rhamnopyranosyl(1 $\rightarrow$ 2)- α -L-arabino-pyranosyl]-28-O- $[\alpha$ -L-rhamnopyranosyl(1 $\rightarrow$ 4)- β -D-glucopyranosyl(1 $\rightarrow$ 6)- β -D-glucopyranosyl] hederagenin, volatile oil (0.5–1.6%), fatty oil (35.6–41.6%), oleic acid, esters of unsaturated fatty acids with C15 and higher terpenoids, esters of dehydrostearic and linoleic acid, aliphatic alcohol, β -unsaturated hydroxy ketone, hederagenin glycoside, melanthin, melanthigenin, bitter principle, tannin, resin, protein, reducing sugar, glycosidal saponin, 3-O- $[\beta$ -D-xylopyranosyl-(1 $\rightarrow$ 2)- α -L-rhamno-pyranosyl-(1 $\rightarrow$ 2)- β -D-glucopyranosyl]-11-methoxy-16, 23-

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